ARRIGE statement on heritable polygenic editing
9 January 2025

One of the seminal events leading to the creation of ARRIGE was the possibility of editing the genomes of human embryos with the CRISPR–Cas9 gene-editing tool. The revelation in November 2018 that a Chinese scientist, He Jiankui, had edited embryos that became living babies raised a consensus condemning it as a failure in scientific integrity because the science did not allow such a precise and safe editing, a failure in medical ethics, because the prevention of HIV doesn't need such intervention, and a failure in public debate that had not even occurred to allow such an intervention. Following that publication, ARRIGE released two statements, in December 2018 and June 2019, discouraging the use of genome editing techniques in human embryos. This has led us to wonder why Nature in its 09/01/2025 issue seems to reignite the debate with an article by Visscher et al. describing a mathematical model that argues for heritable polygenic editing to reduce the risk of several common disorders, developing a theoretical scenario based on an entirely speculative idea that heritable, large-scale genome editing is feasible and safe, which is not, according to the latest advances and innovations of this technology.

Speculation is one thing and the ethics of research needs an open and anticipatory discussion. However, there is no ethics without a strong scientific basis, and imagining in this article the possibility to transfer these polygenic modifications to human embryos is insane and totally imprudent, not to mention being mostly illegal in the majority of our countries. Good bioethical reflections should always begin with good biomedical data. In the absence of scientific evidences those thoughts are merely speculative comments without any solid ground foundation.

The model's reliance on oversimplified and unproven assumptions regarding genetic mechanisms, environmental factors, and population variability significantly diminishes its practical applicability and reliability. Indeed, the model assumes that genome-editing techniques can modify human embryo DNA with flawless precision. Even in three decades from now nothing allows one to make such an affirmation. The approach also relies on accurately identifying causal genetic variants. Genetic-association studies, however, do not directly pinpoint causal alleles but instead identify linked variants with a certain associated probability with a measurable trait, not with certainity. This indirect method has proven slow and fraught with contradictions, especially for well-studied traits, casting doubt on the reliability of the genetic data. The model then presumes that the effects of protective variants are independent and additive. Without data on individuals carrying multiple rare protective variants, this assumption remains unproven. Furthermore, protective alleles' effectiveness may vary across environments and life circumstances, including treatment availability that could render certain protective alleles obsolete. This variability undermines the universality of the model. Finally, the model assumes uniform risk reduction across all individuals, which is unrealistic. This variability limits the applicability and equity of the model's predictions.

In this contemporary era of fake news and alternative truth, such a publication is not only a provocation, it will also feed distrust in scientific activities and remains highly irresponsible.

The ARRIGE Board